IN THE CLAIMS:

Please replace all prior listings of claims with the following listing of claims.

Claims 1-93 (canceled).

Claim 94 (currently amended). A method for quantitative structure function analysis research on biologically active proteins or peptides, said method comprising applying a specific chemical modification of selected amino acids to said proteins or said peptides whereby said modification results in said proteins and said peptides having at least one feature selected from the group consisting of enhanced biological activity, enhanced stability, suppressed antigenicity, acquired antagonistic activity, and cell inhibitory activity, said method comprising:

a) gradual chemical modification of a protein or peptide, followed by

b) monitoring the modification reaction with a mild and sensitive method such as nondenaturing electrophoresis or electrospray mass spectrometry and optionally confirming the overall structural integrity;

c) protease treatment;

d) mass spectrometry; and/or

e) assaying biological activity of the modified product and optionally assaying stability of the modified protein.

Claim 95 (currently amended). The method according to claim 94, wherein said proteins or peptides are selected from the group consisting of interleukins, haemopoietic growth factors, peptide hormones, protein hormones, signal peptides and signal proteins.

Claim 96 (currently amended). The method according to claim 94, wherein said protein or peptide is selected from the group consisting of cytokine superfamily, insulin, and prolactin.

Claim 97 (currently amended). The method according to claim 96, wherein said protein or peptide is a member of the cytokine superfamily selected from the group consisting of interleukins 1-8, interleukin 10, CM-CSF, TNF, gamma IFN and EPO.

Claim 98 (currently amended). The method according to claim 97, wherein said protein or peptide is an interleukin ~~slelected~~ selected from interleukins 1-7.

Claim 99 (currently amended). The method according to claim 94, wherein specific digestion with specific proteases and mass spectrometry is carried out for characterisation and localisation of the modified amino acids.

Claim 100 (previously presented). The method according to claim 94 or 99, wherein specific digestion with specific endoproteases and laser desorption mass spectometry is carried out for characterization and localization of the modified amino acids.

Claim 101 (currently amended). The method according to claim 100, wherein said endoprotease is Endo Glu C or Endo Lys C.

Claim 102 (currently amended). The method according to claim 94 or 99, wherein the modification is carried out by specific digestion with specific exoproteases and electrospray mass spectrometry is carried out for characterisation and localisation of the modified amino acids.

Claim 103 (currently amended). The method of claim 102, wherein the exoprotease is Cathepsine C or carboxypeptidase Y.

Claim 104 (previously presented) The method according to claim 94 or 99, wherein said chemical modification comprises alkylation or acylation, said chemical modification being conducted while gradually varying at least one of the conditions under which said modification is conducted, said conditions comprising a pH in a range between a pH of 5.0 and 7.0, the time for conducting said modification, and reagent concentrations.

Claim 105 (currently amended). The method according to claim 104, wherein the modification is carried out in the presence of phosphate buffer~~, preferably~~ and, optionally in combination with acetic anhydride.

Claim 106 (currently amended). The method according to claim 94 or 99, for the introduction of an antagonistic or cell inhibitory activity, wherein the modification has specificity to one or more residues that are involved in catalytic activity.

Claim 107 (previously presented). The method according to claim 94 or 99, wherein the modification is within or in close proximity to a metal binding center, preferably a Zinc binding center, suitably said residue is a histidine residue.

Claim 108 (previously presented). The method according to claim 94 or 99, wherein the modification further comprises reversibly denaturing the substrate and adding chelating agent to remove the metal ion.

Claim 109 (previously presented). The method according to claim 94 or 99, wherein the modification is specific for one type of amino acid, specific to one amino acid, or is specific for only one amine-residue in the peptide or protein.

Claim 110 (previously presented). The method according to claim 94 or 99, wherein the substrate is human interleukin-3, said method preferably providing interleukin 3 modified only at one or more of the following residues: Ala^{1}, His^{26}, Lys^{28}, Lys^{66}, His^{95}, His^{98}, Lys^{100}, or Lys^{116}.

Claim 111 (currently amended). The method according to claim 94 or 99, for the introduction of an antagonistic and/or cell inhibitory activity, said method comprising disruption of phosphate binding.

Claim 112 (previously presented). A modified signal substance selected from the group consisting of a protein hormone, peptide hormone, growth factor, a haemopoeitic growth factor, an inteferon, an interleukin and a colony stimulating factor with enhanced biological activity, antagonistic activity or cell inhibitory activity, wherein said signal substance contains a modification within or in such close proximity to a catalytic center that it effects a biological or chemical feature.

Claim 113 (previously presented). A modified signal substance being a Zinc binding signal peptide selected from Growth Hormone, prolactin, insulin, and a cytokine acting on the same cytokine receptor superfamily as the IL-3 receptor, said modified substance having been modified in such close proximity to a Zinc binding center that the modified substance has acquired an enhanced biological activity, antagonistic activity or cell inhibitory activity.

Claim 114 (previously presented). The substance according to claim 113, wherein the metal ion is within or in close proximity to a catalytic center that effects a biological or biochemical feature.

Claim 115 (previously presented). The substance according to one of claims 112-114, wherein the modification for producing an antagonist is a chemical modification comprising an alkylation, an acylation or molecular biological modification, wherein said chemical modification includes a deletion mutation or a substitution mutation.

Claim 116 (currently amended). The substance according to one of claims 112-114, wherein the modification is of an amino acid involved in the binding of a metal ion.

Claim 117 (currently amended). The substance according to one of claims 112-114, wherein the affinity of the signal substance for the receptor has not decreased by more than a factor of 10.

Claim 118 (currently amended). The substance according to one of claims 112-114, wherein the substance is interleukin 3.

Claim 119 (previously presented). The substance according to claim 118, comprising at least one of the following characteristics

a) 0.1 ng of the substance, modified IL-3 inhibits up to approximately 50% of 3ng/ml native IL-3;

b) 3 ng/ml of the substance, modified IL-3 suppresses 80-90% thymidine incorporation of 30-100 ng/ml control IL-3;

c) the substance modified IL-3 inhibits control IL-3 by a factor of 10-100.

Claim 120 (previously presented). The substance according to claim 119 which is human interleukin 3 which has been modified at one or more of the following residues: Ala^{1}, His^{26}, Lys^{28}, Lys^{66}, His^{95}, His^{98}, Lys^{100}, or , Lys^{116}.

Claim 121 (previously presented). The substance according to one of claims 112-114, wherein the substance has acquired one of the following combinations of characteristics:

a) a decreased stability and increased antagonistic activity;

b) a decreased stability and increased agonistic activity;

c) an increased stability and antagonistic activity; or

d) an increased stability in combination with an agonistic activity.

Claim 122 (canceled).

Claim 123 (previously presented). The substance according to one of claims 112-114, wherein the concentration of substance required for inhibition is suitable for clinical application, being less than a hundred fold higher than the native substance concentration, said substance optionally further having increased receptor binding capacity.

Claim 124 (previously presented). A method for stimulating stem cell-replication comprising application of a preparation according to claim 118.

Claim 125 (canceled).

Claim 126 (canceled).

Claim 127 (canceled).

Claim 128 (canceled).

Claim 129 (previously presented). A method for stimulating stem cell-replication comprising application of a preparation that is a modified signal substance or a modified signal substance being a zinc binding signal peptide, wherein said modified signal substance comprises interleukin 3 or a substance obtainable according to claim 94.

Claim 130 (previously presented). A method of gene therapy comprising applying a nucleic acid construct encoding a substance according to one of claims 110-112 to a subject to be treated, said thereapy being directed at HIV infection.

Claim 131 (previously presented). A preparation for clinical application comprising a substance according to one of claims 112-114 and an additional signal protein or peptide.

Claim 132 (previously presented). A method for stimulating stem cell-replication comprising application of a substance obtainable according to the method of claim 94.

Claim 133 (previously presented). The method according to claim 94 or 99, wherein said chemical modification comprises alkylation using iodo acetate, or acetylation using acetic anyhydride or using succinic anhydride, said chemical modification being conducted while gradually varying at least one of the conditions under which said chemical modification is conducted, said conditions comprising a pH range between a pH of 5.0 and 7.0, time for conducting said modification, and reagent concentrations.

Claim 134 (previously presented). The modified signal substance according to claim 113, wherein said cytokine acting on the same cytokine receptor superfamily as the IL-3 receptor is selected from the group consisting of IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, GM-CSF, EPO, and IFN-gamma.

Claim 135 (previously presented). The substance according to claim 121, wherein the substance acquiring one of said combinations of characteristics is

a) acetylated IL-3;

b) an N-terminally proteased IL-3;

c) succinylated IL-3; or

d) a C-terminally proteased IL-3.

Claim 136 (previously presented). The method according to claim 108, wherein the chelating is conducted in the presence of urea and EDTA.

Claim 137 (new). The method according to claim 94, wherein the modified protein or modified peptide is a modified signal substance selected from the group consisting of a protein hormone, peptide hormone, growth factor, a haemopoeitic growth factor, an inteferon, an interleukin and a colony stimulating factor with enhanced biological activity, antagonistic activity or cell inhibitory activity, wherein said signal substance contains a modification within or in such close proximity to a catalytic center that it effects a biological or chemical feature.

Claim 138 (new). The method according to claim 137, wherein said modified substance is interleukin 3.

Claim 139 (new). The method according to claim 138, wherein said modified substance comprises at least one of

a) 0.1 ng of the substance, modified IL-3 inhibits up to approximately 50% of 3ng/ml native IL-3;

b) 3 ng/ml of the substance, modified IL-3 suppresses 80-90% thymidine incorporation of 30-100 ng/ml control IL-3; or

c) the substance modified IL-3 inhibits control IL-3 by a factor of 10-100.

Claim 140 (new). The method according to claim 94, wherein the modified protein or modified peptide obtained has acquired one of the following combinations of characteristics:

a) a decreased stability and increased antagonistic activity;

b) a decreased stability and increased agonistic activity;

c) an increased stability and antagonistic activity; or

d) an increased stability in combination with an agonistic activity.

Claim 141 (new). The method according to claim 133, wherein the modified protein or modified peptide is

a) acetylated IL-3;

b) an N-terminally proteased IL-3;

c) succinylated IL-3; or

d) a C-terminally proteased IL-3.

Claim 142 (new). The method according to claim 137, wherein the modified signal substance is modified TNF.